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BULLETIN

OF

THE JOHNS HOPKINS HOSPITAL

Entered as Second-Class Matter at the Baltimore, Maryland, Postoffice.

Vol. XVII.—No. 183.] BALTIMORE, JUNE, 1906. [Price, 25 Cents

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TWO CASES OF STRICTURE OF THE URETER; TWO CASES OF HYDRONEPHROTIC RENAL PELVIS SUCCESSFULLY TREATED BY PLICATION.[1]

By Howard A. Kelly, M. D.,

Gynecologist-in-Chief, The Johns Hopkins Hospital.

1. Stricture of the Vesical Ureteral Orifice and Pouting Ureter.

A number of cases of this extraordinary condition have been reported, but so far as I know, no case has been diagnosed and treated *intra vitam*. The patient of whom I now speak, Mrs. J. W. F. (No. 1787 San.), came to me through the courtesy of Dr. P. M. Hicks, of San Antonio, Texas. She had had one child nine years before, with a difficult instrumental labor associated with a bad laceration. About six months before I saw her, she had suffered with a bad attack of lower abdominal pain, accompanied by a temperature of 102° and much tenderness in the right side. Since that time she continued to complain of backache and much pain in the lower abdomen. Vaginal examination, Dr. Hicks wrote me, revealed a retroflexed uterus and a somewhat fixed tender mass about the size of an egg in the right cul-de-sac.

November, 18, 1904, I made an abdominal incision and found both ovaries small and sclerotic, 2½ by 1 cm. and 2 by 1 cm. and the ureters appeared normal. The appendix was removed and the uterus suspended. She made a good recovery from this operation but continued to have more or less discomfort in the lower abdomen. Upon a careful bimanual examination November 23, 1904, I was unable to feel anything upon the left side, while the ureter could be felt on the right through the somewhat senile vaginal wall. Upon making a vesical examination in the knee breast posture the bladder distended well, and the posterior wall dropped 6.5 cm. from the anterior wall. Through a number 10 speculum a curious teat of tissue could now be seen hanging down into the bladder from its base on the right side occupying the position of the ureteral mons. This at first appeared as a short truncate cone about 1.5 cm. in diameter at its base, and 6 mm. from base to apex. From the apex clear urine fell steadily drop by drop. While I was in the act of watching it, a remarkable transformation took place; the cone began to swell and in the act of swelling was forced down into the lumen of the bladder; as it continued to grow larger its walls appeared paler, thinner, and clearer, until at the maximum a few red vessels could be seen coursing over the surface, which looked like a large cyst as big as the end of the thumb, full of water. With this distention the flow of urine increased in amount. Numerous translucent areas were visible scattered over the now hemis-

[1] Read before the Johns Hopkins Hospital Medical Society, February 19, 1906.

pherical enlargement, which was from two to three times the size of the eminence originally observed and more rounded in form. Following this distention the cyst collapsed to its former size. I continued to observe it, and noted a periodicity of from 5 to 10 seconds between the intervals of advancement and retraction of expansion and contraction.

The ureteral orifice could fortunately be seen on the anterior inner, or urethral side of this mons, faintly outlined, forming a narrow slit not open at any time.

The left or opposite ureteral orifice lay in a red mucous vesical fold not prominent in its normal position. When the mucous tissues about the right ureteral orifice became distended, the little narrow opening instead of advancing towards the median line of the bladder, remained relatively nearer to the base until the orifice came to lie wholly on one side.

We had here manifestly to do with a stricture of the vesical orifice of the ureter affecting only its mucous surface.

Treatment.—The treatment was very simple. I took a delicate pair of vesical scissors, working on long parallel handles like an alligator forceps, and introduced one of the points into the ureteral slit-like orifice when the sac was fully distended and cut a slit 5 mm. in length. 15 cc. of urine at once gushed out and later 60 cc. escaped, about half of which was estimated to come from the bladder, when the patient assumed a kneeling posture. When examined five days later the right ureteral orifice appeared stellate, widely opened, seated on a red papillary eminence. On introducing a searcher the margins could be readily lifted apart. The opening now looked like a black hole in the bladder wall, instead of a slit situated on the side of a cyst. The patient was discharged well February 9, 1905.

C. Adrian has reported a case of intermittent cystic dilatation of the vesical end of the left ureter (Arch. f. klin. Chir., 1905, Vol. 78, p. 588). The patient had had dull pains in the upper abdomen and in the region of the right kidney, becoming more distressing upon standing or walking; these finally became so intense that she could not sleep. A diagnosis was made when the cystoscope was used; this revealed an intermittent cystic dilatation of the vesical end of the left ureter. The condition was relieved by making a suprapubic opening of the bladder, with an incision into the little mucous tumor, with a suturing of the vesical and ureteral mucosæ with fine catgut.

Adrian calls attention to fifty-two cases of dilatation reported in the literature in twelve of which the diagnosis was made *intra vitam*. See further literature in Th. Cohn (Beiträge z. klin. Chir., 1904, Vol. 41, p. 45).

2. Stricture of the Upper Ureter Treated by Dilatation.

Mr. R. A. W. (San. No. 960), age 42, was under my care for one month from June 10, 1900. He had had repeated attacks of severe pain in the left side seriously interfering with his occupation, which was that of an evangelist. These attacks began January 8, 1879, when he had a long spell of sickness, associated with a bowel trouble thought to be intussusception. The attacks were clearly renal in their origin and as nothing was found by a physical examination or an examination of the urine, I exposed the left kidney and by rotation brought into view a large hydronephrotic pelvis of about the same size as the kidney itself. It was fusiform in shape and extended down below the lower pole of the kidney a short distance beyond the pelvis. The ureter which began normally, suddenly contracted until it was only about 2 mm. in diameter at a point 2 cm. below the pelvis. There were no signs of any adhesions, or evidence of previous inflammation. The pelvis of the kidney, however, was thick-walled, owing to physiological hypertrophy.

Treatment.—Realizing that it was impossible to do any plastic operation on so delicate a structure, I tried that which seemed to be the only feasible plan. I incised the pelvis of the kidney about a centimetre above the ureter and then through this orifice I introduced metal catheters which I have had made for dilating structures of the lower end of the ureter; with these I gradually dilated the stricture until a catheter about 5 mm. in diameter was passed with some apparent rupture of the inner coats of the ureter. The wound in the pelvis was then closed with fine silk and the kidney returned to its position with a small drain. He made a perfect recovery from the operation and has never had any pain from that day to this.

3. Two Cases of Hydronephrosis Treated with Plication of the Renal Pelvis.

The first case was that of Mrs. G. P. (San. No. 1927), 48 years of age, admitted May 10, and discharged June 13, 1905. She had two children, 26 and 15 years before, with normal labors. For the past six years she had been suffering at irregular intervals with acute lancinating pains in the right lumbar region associated with the development of a tumor the size of an orange and very sensitive to touch. The disappearance of the tumor was followed by an increase in the amount of urine.

After placing the patient in the knee breast position, I catheterized the right ureter and injected 135 cc. of a boracic aniline solution which served to bring on the same pains as those of which she had been complaining. The diagnosis of hydronephrosis was thus made positive and an operation advised. At the operation an oblique incision was made 10 cm. in length from a point over the last rib extending downward and slightly outward. I exposed the kidney through my usual route by opening and bluntly drawing apart the fascia forming the superior lumbar triangle lying just below the rib and bordering upon the upper part of the quadratus muscle. The kidney was found extremely movable, and the pelvis, which had been previously distended, was seen to be the size of an after-dinner coffee cup. The ureter was attached to the side of the pelvis at a point 3 cm. above its lower pole. The fatty capsule was separated from the posterior part of the renal pelvis which was then emptied of 62 cc. of fluid through the renal catheter. I then cut away the fatty capsule from the

upper to the lower end of the pelvis and used the remaining portion to sew the capsule together so as to constrict the pelvis, by passing three silk sutures, two mattress and one interrupted, through the margin of the kidney on one side and out into the fibrous tissue of the amputated fatty capsule on the other. When I tied the sutures thus passed, the pelvis was constricted as in lacing up a corset.

One might think that the delicate tissues of the capsule would easily tear and permit a redistension of the pelvis. The tissues proved, however, to be far firmer than I had anticipated, affording a secure snug closure for the pelvis. The ureter was by this means restored to its normal relations, and on pressure on the pelvis, urine was seen to escape downwards without hindrance. The kidney was then suspended by one silk suture around the last rib, and by two others to the quadratus muscle. The patient recovered and was seen by Dr. Hunner six weeks afterwards, who again injected the kidney and found it held only 18 cc.

My next case of plication of the pelvis of the kidney for hydronephrosis, was entrusted to my care by Dr. George Guthrie, of Wilkesbarre, Pa., December, 1905. Mrs. M. J. C. (San. No. 2034), 31 years old, had had one child, after a long, hard labor. During her pregnancy in the fifth month, she was seized with severe pain in the right side followed by the discharge of large amounts of pus in the urine, with albumin which had not been found before. She had suffered from weekly attacks with her kidney from this time until the child was born; after that event the attacks had been monthly. During an attack a tumor would form on the right side which would disappear accompanied with the discharge of pus by the bladder. She had been seen by several other consultants who had found a pyelitis of the right kidney. Dr. Guthrie had also determined the presence of a right pelvic peritonitis with adhesions, and a chronic appendicitis was suspected.

In my investigation I found that there was no stone in the kidney, and there were no tubercle bacilli. I catheterized both kidneys and discovered a mild pyelonephrosis on the right side, the pelvis of the kidney holding 80 cc. of aniline solution. On the left side I found what had hitherto been unsuspected, a much dilated renal pelvis of a capacity of 35 cc.[2]

I then did the following operations:

Dilatation and curettage for an excessive menstrual flow.

Restoration of the broken down vaginal outlet.

Removal of the vermiform appendix.

Removal of the inflamed adherent right tube and ovary.

Shortening the round ligaments by attaching them to the posterior surface of the uterus.

Both kidneys were then operated upon, including:

Plication and fixation of the right kidney.

Plication and fixation of the left kidney.

The kidney was exposed through the loin by an incision similar to that used in the last case. The large flaccid pelvis with thickened walls was then reduced in size by plication, by passing three silk sutures so as to gather up the entire pelvis in a V shape, one inside the other and only on the posterior surface. Each suture started by transfixing the margin of the kidney surrounding the pelvis, and was then carried down into the pelvis towards the ureteral orifice, picking up the tissues of the pelvis, without penetrating the mucosa, and catching the strong peripelvic fascia as in the last case, on the extreme edge of the pelvis. The suture then returned and emerged on the margin of the kidney. After passing three sutures in this way, they were drawn up, so as to pucker and draw the pelvis together, when they were tied, each to its own end respectively. After completing this operation the kidney was suspended as described in the preceding case.

A similar procedure was adopted on the left side, except that two sutures were used instead of three for the plication. The patient made a slow but satisfactory convalescence, and left the hospital after 10 weeks, having gained about 8 pounds in weight and feeling well. There were a few leucocytes in the urine. The kidneys could not be felt at all and there was clearly no accumulation of urine in the pelves. By this operation I feel that I have saved a kidney attainted with a mild pyelonephrosis. I realized that there was some risk in treating a much damaged affected kidney in this way, but I felt that it was well worth the effort in view of the condition of the other side.

[2] I want to call especial attention to this method of determining the presence of hydronephrotic kidney as well as of measuring the degree of the hydronephrosis. The advantages are very manifest. The hydronephrosis is noted in its earliest stages. The exact degree of the hydronephrosis is measured both by injecting the kidney to the point of tension distinctly felt at the syringe as well as to the point of bringing on some pain in the pelvis of the kidney. It is also determined by collecting the fluid which escapes from the kidney as soon as the injecting instrument is removed.

THE USE OF QUININE DURING THE CIVIL WAR.[1]

BY JOHN W. CHURCHMAN, M. D.,

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If coffee, cathartics, and ammunitions were the sinews of the Civil War—arranged in order of importance—quinine was the staple that would have been, after these three and perhaps after whiskey, most missed. In the early days of the century, when surgery was still so largely a question of fractures and emergencies, and when medicine was only beginning to know the interest and advance which were to come with applied microscopy and chemistry and physics, quinine was arousing

[1] Read before the Johns Hopkins Hospital Historical Club, May 8, 1905.

a lively interest indeed. And it was an interest destined to continue on through its seventh and eighth decades.

From that pride and scandal of medicine—the Surgeon General's catalogue—one may obtain a fair idea of the attention this drug was demanding in the days when the Missouri Compromise and the policy of the Free Soilers, and the Omnibus Bill were the vital things, and Henry Clay and Dred Scott and John Brown the names in the headlines. The literature of the subject rapidly took on dimensions. Articles appeared on almost every conceivable phase of the question. Inaugural theses and ephemeral articles were written on the pharmaceutical preparation of the drug, on the procedure of extraction, on its detection in the urine, on quantitative and qualitative chemical analysis, on the solubility of its salts. Elaborate dissertations appeared labeled, "On the Sulphate of Quinine." Historical studies were published, the beautiful Countess of Chinchon always appearing in one of the early acts. Search for febrifuges to be used as substitutes was instigated, experimental work was carried out as to the action of the drug on this organ and that. Methods were published for the recognition of adulterations. Quinine salts, from the arseniate to the valerianate and back again, came to the fore. Learned discussions took place as to its action on the uterus and to decide whether it were an oxytocic, an ecbolic, or a partus accelerator—a question which seems to have kept the profession awake nights in the 70's and 80's. Then its dosage was discussed; and methods for disguising its taste invented, and new routes for its administration suggested and accidents following its use reported. Even the surgeons looked to the drug with hope and articles appeared on its antiseptic value and application to surgery. But clinicians were the chief contributors; and the drug was administered in nearly every disease known to man. Convulsions, erysipelas, neuralgia, rheumatism, typhoid, yellow, malarial, and puerperal fevers—these were only a few of its indications. It was used for its effect on the pulse, it was used topically, it was used to reduce an enlarged spleen. It was advised by one observer in "brain disease," and its power in accelerating the action of mercurials was lauded by another. The diseases of childhood seemed to indicate it particularly and "the quinine rub for children" was lauded in a French article.

Even the followers of Hahnemann contributed to the discussion; and it was really little wonder that before long "abuse" began to take the place of "use" in the titles and that a generation of practitioners had sprung up trained to transform their patients' mouths into funnels gaping for quinine.

But for the military interests of the nation an added attention had been given to this drug by the experiences of the strife waging with the Seminoles during the early 40's.

Florida, the scene of this distressing and protracted warfare, was hardly the best State into which to send soldiers unless the supply at home were unlimited. It was the State of hammocks and savannas, of disappearing lakes and streams, of lime-sinks, bay galls, and bad water. From May to August the rain fell in torrents. The humidity was great, the dew-point high, the mean temperature from 80° to 82°. Lake Tuscawilla suddenly disappearing subterraneously in 1838 and leaving a mushy bog behind it, Lake Orange gradually passing from sight throughout several years—these were samples of what not unusually happened. "A dead level," said a medical writer of the time, "and a half drained country alternately drenched with rain and broiled by an almost tropical sun—reeking with the steam from ten thousand swamps, lagoons, bogs, and savannas—would furnish ample materials for vegetable decomposition and miasmatic effluvia." And such material was indeed furnished. "All fevers of malarial origin"—intermittents, remittents, congestive fevers, dysentery—prevailed throughout the State. The first sign, indeed, of residence in Florida—so it was said at the time—was the cutaneo-hepatic sympathy of Dr. James Johnson; an increase of perspiration with an increase and vitiation of bile. Then followed a series of symptoms characterized by increasing malaise, impaired digestion, growing irritability, pallor, languor, and tendency to venous congestion; leading, in the end, to a frank attack of fever—the two never-failing signs of an oncoming attack being peculiar sensations in the right hypochondrium (attributed to hepatic engorgement) and the passage of dark red urine, small in amount. Finally when the attack was over the patient who had brought a vigorous constitution from the north, was left permanently pale, languid, with a poor digestion, torpid liver, muscular debility, and great susceptibility to atmospheric changes. Such was the attraction offered to immigration. And this state of affairs existed not only in the regions of marshes. Malaria was noticeably present in the barren and sandy portions as well—its presence being explained at the time by the geological character of the soil which was studied in great detail. The prevailing northwest winds were also held to account for much of the disease—a pretty distinct relation being established between the occurrence of miasms and the land breezes. Also the drinking of water in the limestone and alluvial regions must, it was thought, have some etiological relation to the diseases; for had not Dr. Rush said, "There can be no doubt of the predisposition to fevers being increased by the use of impure water," and could it be otherwise? So miasma and impure water did valiant scapegoat service while the real sinner went all unrecognized, close at hand. "During the summer season," wrote Dr. Little, describing conditions in middle Florida, "our ears are assailed by the buzzing of myriads of mosquitoes in their murderous attacks. So formidable are their stings that cattle and deer are often compelled to leave the swamps and take up their residence in the pine woods to avoid them." With dead level, then, and a country half drained, with drenching rains and a broiling sun, with marshes and bogs and lagoons, with favorable wind and soil and unfavorable water, with myriads of murderous mosquitoes doing deadly work, it was no wonder that malaria, as Assistant Surgeon Porter put it, was "the great primary and specific cause of most of the diseases of Florida." And so, indeed, the recruits from the North—

sent to this miasmatic morass to undertake for the Government the exceedingly trying and hazardous task of playing at hide and seek with the Seminoles—found the facts to be. But clinical lessons were learned to prove of national value later. Bleeding in malaria, for instance, was found to be injurious—universally and decidedly; and the favorite panacea was generally abandoned. Cathartics, given as a part of routine prophylaxis and as an adjuvant to quinine, were found extremely beneficial; and Porter's statement that they are particularly well borne by soldiers is easily believed when we learn that 8-10 grs. of calomel followed by oleum ricini, or 15-20 grs. of calomel alone were no uncommon dose. Tamarind water was found to be the best nourishing drink, rarely disagreeing with the stomach, always grateful and never causing the gastric pain and vomiting which occurred when limes or lemons were used. The value of capsicum was also amply demonstrated. But the *great* clinical lesson of the war was what it taught of quinine—establishing in part the wisdom of certain methods for its use, in part only corroborating what others had previously suggested. The reports made came chiefly from two United States posts—Fort White and Fort King. At the former, in the very unhealthy summer of 1839—when fevers were prevailing throughout Florida and yellow fever on the coast—"malarial" diseases occurred in number; but the only fatal cases were two, one from congestive fever and one from cholera infantum: a result to be ascribed, said Surgeon Porter, "almost entirely to the use of quinine in pretty large doses (8-10 grs.) early in the disease." In 1840, the year following, the rainy season was prolonged, 90 inches of rain fell at Tampa Bay and the general health of Florida improved. Yet the troops in the interior suffered severely from fever, diarrhœa, and dysentery. At Fort King an epidemic broke out which involved nearly every man, woman, and child in the post. Two hundred and seventy patients were taken sick in April and May—and this in a garrison four infantry companies strong. Here was an opportunity to study the disease at close range; and Surgeon Porter improved it. He prescribed quinine and he prescribed it in large doses. Chamomile tea, capsicum, and cathartics were used unsparingly but quinine was given and given in confidence. It was ordered at the onset of the disease (grs. xv-xx-xxv) and it was repeated p. r. n.—"quinine sulphate ℈ ss̄" appearing frequently in the medical orders. Here is the way drugs were handed out to these patients—being excerpts from the clinical notes on a Lieutenant of the 2d Infantry:

"3 p. m.—Slight attempt at perspiration which soon subsided and at retreat the symptoms were the same as at 1 o'clock, with the addition of great restlessness and uneasiness. ℞ hydrarg. chlor. mit. gr. i, pulv. antimonialis gr. ii, morph. sulph. gr. ¼. *To be continued at intervals during the night.*" (The italics are mine.) The next morning, the clinical clerk who must have had a grim sense of humor, made this note: "Obtained some sleep during the night." Quinine treatment (grs. xv) was instituted. On the 17th the 1 p. m. order was "No medicine:" and at retreat the significant entry was made, "Has been in a quiet sleep." The simple life was, however, not to continue and at tattoo this strenuous order was left: "℞ hydrarg. chlor. mit. gr. i, pulv. antimon. gr. ii, morph. sulph. gr. ¼, a seidlitz powder at 2 a. m. and 10 grs. of quinine at reveillé." The patient recovered. Not only was quinine found to prevent the paroxysms and cure the patient but it seemed, combined with capsicum, to be the best remedy for the distressing gastric irritability—particularly marked among the recruits—which was apparently so important a feature of the disease. "The paroxysms," a medical writer before the Seminole War had written, "continue to recur until either a salutary crisis or death takes place—one or the other of which not infrequently occurs in the third paroxysm." But this was with the ordinary treatment in which quinine was used only as a tonic late in the course of the disease; and the experience of the army physicians with quinine showed that such a fatalistic philosophy was not warranted. The drug was used by them in ten times the usual dose not as a tonic but as "*the certain antidote;*" convalescence was "immediate and invariable;" and "the termination by crisis," to quote Surgeon Porter, "was created rather than awaited."

To the world-wide medical interest, then, in malarial conditions and in quinine manifested in the first decades of the 19th century, the trials and successes of the Florida war had added an interest that was provincial and national; and when Fort Sumter fell, the dreadful diseases for which quinine was to be needed must have loomed large in the medical minds which were planning for a disagreeable and uncertain future and to which the absolute necessity of this staple of war must have been distressingly apparent. For the drug, as was to be expected and as the event proved, was to be the chief reliance in two of the largest groups of disease during the Civil War—the alvine fluxes and the camp fevers.

The alvine fluxes, according to the official nomenclature, included the acute and chronic diarrhœas and the acute and chronic dysenteries; and they were, indeed, the bane of the armies. The statistics are little short of amazing. The fluxes were more frequent and produced a greater mortality than any other disease. They were responsible for about one-half of all the cases of sickness and caused, with scurvy, 831 of every 1000 deaths from disease. They appeared at the beginning of the war and in regiments before organization. It often happened in the hospitals that more were sick from dysentery than from all other causes; and when it is remembered that the proportion of deaths from disease to the deaths from wounds was about as two to one among the whites and as over eight to one among the negroes, the tremendous economic problem this disease presented becomes apparent. In the white and colored troops of the North from the beginning of the war to June 30th, 1863—that is before Gettysburg had been fought, or Vicksburg had fallen, or the draft riots had been quelled in New York—nearly 1,800,000 cases had been recorded under one of the four alvine fluxes; and, at a conservative estimate, almost 60,000 soldiers had died from the disease. The Union had lost, from dysentery, in other words,

an army twice the size of the garrison which made Grant famous by surrendering to him, over five times as many men as the killed and wounded at Chancellorsville; troops equal to about three-fourths of the forces which turned the tide of the war by repulsing Lee's invasion of the North. In three Indiana regiments alone, representing a strength of 3000 men, the reports, though exceedingly incomplete and including only a part of the war, list 1567 cases of dysentery. The number of those on sick report for the fluxes was to the total of all diseases as, approximately, one to four. For the single year ending June 30, 1863—the year that began with the Emancipation Proclamation and ended with Lookout Mountain—nearly 522,000 cases of dysentery were reported with 10,554 deaths. Yet Chancellorsville was called a terrible and sanguinary conflict. In the Confederate Army similar conditions were prevailing. From July, 1861, to March, 1862, the Army of the Potomac with a mean strength of about 50,000, reported over 36,000 cases of alvine flux—740 cases, that is, to 1000 of mean strength; and no doubt the medical records, destroyed at the fall of Richmond, would have shown a similar state of affairs throughout the war. The disease, said Surgeon Jones, "destroyed and injured permanently more men than shot and shell." At Capt. Wirtz's notorious Andersonville prison for about 15 months during '64 and '65 nearly 18,000 prisoners were admitted to the hospital. Four hundred and fifty odd of these were wounded and about 16,000 suffered with a specified disease. The results were recorded in about 15,000 cases and the mortality was 73.7 per cent. Over seven thousand cases of diarrhœa were listed; and, excluding cases not followed, 80.3 per cent of them died. In other words in a hospital with 18,000 medical and surgical patients admitted during a short year and a half there were over 5000 known deaths from alvine flux alone.

To combat this wide-spread contagion quinine was, of course, not exclusively or perhaps chiefly used. Ipecac and a whole host of other drugs were the stand-bys. But Peruvian bark and what Dr. Woodward calls its "precious alkaloid," were extensively ordered. The drug had been used with good results by Richard Morton in the London epidemic of 1666 and later by York in 1709. Moreover dysentery was still vaguely thought of as a "malarial" condition and that was indication enough for quinine. And so it was prescribed; prescribed for the prostration accompanying dysentery, for the debility of convalescence and for the cases complicated with malaria; it was even in some cases prescribed to excess; but these errors said Dr. Woodward, were "among the most pardonable and least injurious of the therapeutic errors of the Civil War."

But the chief call for quinine came, of course, from camp fevers; and it was a loud call, and a strong, and a constant. The camp fevers of the war included typhus and typhoid, common continued fevers (after June 30, 1862, reported as "other miasmatic disorders"), remittent fever, quotidian, tertian, and quartan fevers, and congestive intermittent fever. The question of diagnosis was, of course, still somewhat unsettled. Even typhus and typhoid were not clearly distinguished. The work of Louis had, indeed, appeared in 1829; Gerhard and Pennock had published in 1837, Shattuck in 1839, and Bartlett and Wood in the early 40's. Yet Dickson, of Charleston, as late as 1855 quoted from Campbell with approval, "The necessity which any theory may involve of separating typhus gravior and mitior is enough of itself to declare its absurdity;" and of the three text-books furnished the medical officers during the war (Wood, Watson, and Bennett), two were non-identist and one monistic. Of course the diagnosis was made entirely from clinical features; and though certain cases of typhus probably got into the typhoid statistics the error was apparently not a large one. As to "typho-malaria," however, there was much confusion. The term was introduced by Woodward in 1862 for those hybrid fevers which he thought due to a combined poison—modified, in some cases, by a "scorbutic taint." He hoped by this innovation to clarify the diagnostic atmosphere; but he succeeded in befogging it. The terms came to be used by the army surgeons to include those febrile remittents which assumed the adynamic form present in enteric fever, and enterics with malarial complications. *True* malaria—remittent and intermittent—was pretty well recognized. But it is, of course, in the statistics of the aggregate camp fevers and not in the statistics of the separate groups, that we are interested; and, as in the case of the alvine fluxes though less notably than in that case, the figures are huge. One quarter of all the cases of disease among the white troops were of a malarial character. This does not include a large number of cases complicated with pneumonia and other diseases and reported under those headings. Nor does it take any account of the great number of recurrent cases which were treated by the men themselves—who recognized and became used to ague fits, took quinine and were simply excused from duty by their company officers without reporting to the surgeons. Yet even so, consider the extensive ravages of the disease. From May, '61, to June, '66, over 1,100,000 cases of pure malaria and nearly 50,000 of typho-malaria were reported among the white troops. Of these 12,199 died. In other words there were 2814 cases of malarial disease and over 26 deaths from malaria per 1000 of mean strength. In three years of service nearly 160,000 cases, with over 3000 deaths, occurred among the colored troops. In the Confederate Army of the Potomac (roughly 50,000 men strong) 1865 cases of malaria occurred between July, 1861, and March, 1862; and at Andersonville in about six months, there were 3000 cases and 119 deaths.

But the camp fevers, so rife throughout the war, made for themselves, a special name and fame in the second twelvemonth. The year was 1862, the Bull Run fiasco had been almost forgotten, Scott had retired and McClellan was looming as the most important military figure of the Unionist forces in the East. The giant North, having stood at gaze for some months had taken a few slumbering and blundering steps forward and was now beginning to awake to the true significance of things; but meanwhile the alert David, with a

sling and a few smooth stones from the brook, had been doing telling though not fatal work. "On to Richmond" had been the cry at the North during the winter; and in the spring McClellan responded. On account of transportation facilities he chose for his famous campaign that famous strip of land lying between the York and the James. Here it was that the colonies had gone to childbed to be delivered of the nation; and here Lafayette, Cornwallis, and Washington had seen her travail pains, and her rejoicings that a son was born into the world. Through this historic ground McClellan pressed until, by the close of May, he found himself within seven miles of Richmond. Then came the news that expected reinforcements could not be sent and the Army of the Potomac was left to its own resources in the Chickahominy Swamps. Malaria and typho-malaria—familiarly called "Chickahominy fever"—soon became prevalent. Meanwhile Stonewall Jackson had joined Light Horse Harry Lee's son—who was now rapidly forging to the front; and McClellan's thin and fevered army was gradually pushed back by July 1, to Malvern Hill. Richmond was safe and Lee was able to assume the offensive. The Peninsula which had perpetuated the names of Washington and Lafayette and Cornwallis as soldiers, which had tested the mettle of McClellan and had insured the fame of Lee left also its mark in medical history by adding to its nomenclature "Chickahominy fever" and by emphasizing the great disabling power of this disease.

The drug that had to be provided for this second widespread group of diseases was the drug which was being used so extensively in the alvine fluxes; but do not suppose it to have been an entirely settled question, at the outbreak of the war, that quinine was a malarial antidote. Peruvian bark had indeed been so regarded by Lind as early as 1765, and also by Hunter, Clark, and others. But James Johnson, in Calcutta, had re-introduced venesection; and though quinine had been discovered in 1820, Sir J. Martin—writing as late as 1861—said, "Quinine, the great febrifuge acts * * * purely as a nerve tonic to the cerebro-spinal and visceral sympathetic system," and "bleeding * * * is very generally necessary in the severer forms of Bengal remitent fever; then come full doses of calomel and sudorifics short of producing salivation, with saline purgatives, antimonials and refrigerants and quinine in the intervals." At the same time, however, Hare, in India, was using the drug in large doses and as an antidote; and in 1836 Maillot, in France, from a study of many thousand cases spoke of laxatives and purgatives in malaria as obsolete ideas and concluded that quinine should always be used. "All the morbid phenomena," said he, "will disappear as if by enchantment in a few hours." Ten years before this, Perrine, treating the disease in Mississippi, had used and advocated quinine strongly; and it seems probable that he was the first to insist on large doses. Surgeon Harvey, however, in the Florida war had been one of the early extensive users and staunch advocates of the drug; and the result of all this was that, when the war cloud really broke, quinine, though there were still prominent dissenting voices, was regarded as the specific drug for malaria and became, as a matter of fact, the *sine qua non* throughout the strife, practically no other antiperiodics being used. Even "prophylactic quinine" was recommended in the "Rules for Preserving the Health of the Soldier," published by Van Buren in 1861; so that there can be no doubt as to the fact that the treatment of malaria was then fully understood.

I have said nothing, in calling attention to the terrific dimensions of the camp fevers and the alvine fluxes during the war, of the sub-acute and chronic distress they occasioned; yet, as a matter of history, this feature was quite as marked as the more acute manifestations. For war—the typhoid of nations—resembles its clinical prototype not alone in bringing prostration, depression, and suffering, nor in exacting a high bounty of life. It is like it in this other respect, too, that it collects its usury in long continued instalments, leaves behind, for days after defervescence and convalescence, reminders of itself in the shape of debility, distressing sequelæ, and a motley array of disabilities. One thinks, for instance, of the march of the army of Charles VIII through Europe in 1494, with the conquest of the Italian Peninsula in contemplation and a highly pious ambition to reach Jerusalem; but ending by making the name of Fracastorius' shepherd a household word throughout Europe and starting it on its way toward Persia and Turkey and the Orient. What indeed, for the common weal of Europe, or of the world, were the paltry lives lost on the march? A continent syphilized—here was the real ravage of an army; and that same continent, feeling keenly to-day the distressing and disabling sequels of the acute fever which it has now well-nigh forgotten, illustrates what distress a war can set in motion. Or a few French soldiers buried in Algiers: was *their* loss a national calamity? A calamity, at least, at all comparable to the army's introduction, on its return, of a new febrifuge which turned out to be the baptism—or better—the immersion of French national progress in absinthe? Some day the full story of the late effects of war will be written; and it will be an illuminating chronicle. Of our own intestine upset it is, of course, even yet not uncommon to see the sequelæ in wrecked constitutions and disabilities of every nature; but if we needed any other reminder of the state of affairs than the Pension Budget we would find it in a glance at the statistics of war times. Look, for example, at the facts as to diarrhœa and dysentery. Seventeen thousand three hundred and eighty-nine white soldiers were discharged from the fighting army on certificate for disability due to these two diseases; and a very large number of the 15,000 discharged for "debility" were really dysenteries. So also were a large proportion of those discharged for anæmia, dropsy, etc.; and of the great number of dysenteries mustered out at the end of the war and not entered on the reports we shall never have any accurate conception. So, too, as regards malaria which was the real cause of a large proportion of the, approximately, 102,000 general debilities and miasms, of the 21,872 anæmias, of the nearly 8000 dropsies reported; and when we learn that almost

15,000 white soldiers were discharged for "debility" alone we realize what a tremendous feature the late results of malaria were.

Here then were the elements for a good quinine market when the war came. A widespread medical interest in the drug, a strikingly successful national experimental test of it fresh in the medical mind, a prospect of the wide prevalence of one disease calling loudly and of another calling exclusively for it—these things meant that much quinine would change hands between 1861 and 1865. And much *did* change hands. The Purveyor's Report for the war lists the purchase of about 393,000 dozen quinine sulphate pills; of over 500,000 oz. of fluid extract of cinchona; of 260,000 oz. of powdered calisaya bark; of nearly 600,000 oz. of quinine sulphate; or, briefly, a total of over 19 tons of quinine sulphate, and over 9½ tons of sulphate of cinchona—beside other preparations. Compare this with the 220,000 quarts of castor oil bought; with the 683,000 dozen c.c. pills; with the 515,000 pounds of Rochelle salts, and you will see that quinine was, indeed, as I have already said, playing Romeo to cathartic's Juliet. In the Confederate camp, too, the drug was used in quantity. It was a contraband of war; but it got through. Not, however, in sufficient amount. Nor could it be brought from Europe past the blockade; and Dr. Jones found it necessary to urge a search for an indigenous substitute, which was, strangely enough, to make the South independent of the North not only during the war but afterward, when she had become an established nation. Georgia bark and dogwood were both tried in this extremity; and both proved failures.

So much for the probable needs and the actual demands of the two armies in regard to quinine. To whom was the government to look for the tremendous supply required? On August 29, 1904, William Weightman, popularly known as the richest man in Pennsylvania and certainly one of the largest real estate owners in the country, died in Philadelphia. He was a singularly reserved man, a captain of industry, a practical scientist of rank; a man of sagacity, energy, and thrift, who amassed a fortune of at least $50,000,000 and died in the harness. Eminently fitted to serve the community he had little in common with it, finding his chief interests in the making of a fortune and the raising of chrysanthemums to a variety of which his name became attached. He owned more property in Philadelphia than the Pennsylvania or the Reading Railroads. The Garrick Theatre and the Hale Building—assessed at $2,000,000—were two of his holdings. He made it a point never to sell any of his properties—the only exception to this rule being the sale of the Bingham House, which brought him $1,000,000. The store of Darlington & Co. belonged to him; whole blocks in Philadelphia were his; and his personal property tax return for 1903-1904 was over $5,000,000. Here we find, then, the resting place of the dollars that went for those 19 odd tons of quinine and of the many thousands of dollars that followed them when the monopoly established during the war lived on and grew fat. At the outbreak of the war there were but two chemical houses in the country engaged in the manufacture of quinine from Peruvian bark. Powers & Weightman, and Rosengarten & Sons, both of Philadelphia. Previously the properties of the bark had been obtained by a process of suffusion; but these two firms, quickly introducing the method for separating quinine—invented by the French chemists, Pelletier and Coventon in 1820—were soon without successful rivalry in the American manufacture of the drug. And before long the price of the drug ($2.10 per ounce at the outbreak of the war) was, by reason of this monopoly aided by certain economic conditions, soaring heavenward. Alcohol, the essential solvent of quinine carried a heavy internal revenue tax; so that a duty was placed on imported quinine sulphate in order to allow the American drug to compete with that imported from Germany and other countries where alcohol was free. The duty was 45 per cent; but the government, buying its quinine duty free, was able to avoid the monopoly of the American firms. Not, however, until large bills for the drug had been incurred. In New York alone nearly $591,000 were spent for quinine, $418,000 of this going to J. H. Reed & Co., who were customers of Powers & Weightman; and the payments made to the latter firm themselves for drugs and medicines during the war amounted to over $231,000, of which a large share went for quinine. But, though the records of these transactions are, obviously, not complete in detail, the Confederates, too, were swelling the bank account of the northern Trust. The drug was contraband and had to be shipped South minus all markings. Moreover Powers, the head of one firm, was a loyal and ardent Unionist; while Adolph Rosengarten, a member of the other, was killed at Murfreesboro after having risen to the rank of major in Anderson's Cavalry. Yet the South got its drug—stored on one occasion in mattresses; and it paid for it, at one time as much as $15 an ounce.

After the war, however, the firm, though becoming fabulously wealthy, began to become extremely unpopular as well. The war duty on the bark had been lifted in 1870; in 1872 the duty on the sulphate had been reduced to 20 per cent. Yet the Philadelphia firms became by no means lean kine. The monopoly, it began to be rumored, was being overdone; the tariff-tax on quinine, prohibiting the sick-poor from using the drug, was grimly nicknamed the "tax on blood;" what had been termed business sagacity began to look like scandalous greed; and a popular cry for redress sounded. Even the *New York Tribune*, the most rabid high tariff newspaper in the country, fought valiantly for repeal; and finally the Government yielding to the country's importunity removed the tariff on quinine under the Dingley bill of 1897. Meanwhile the drug has become immeasurably cheaper. Cinchona has been transplanted to Java, Ceylon, and India, where it grows so extensively that the supply exceeds the demand. Improvement in cultivating the bark has resulted in doubling the yield of quinine to the pound of cinchona. Solvents other than alcohol have come into use—fusel-oil and coal-tar chiefly. And the quinine of commerce—which was quoted in 1861 at $2.10 the

ounce and brought as high as $15.00 below the line—sells for 21 cents an ounce.

Looking ahead then to our next civil, or perhaps colonial, war, it does not seem likely that the quinine problem will loom large. The question of duty has been settled; and even if this were not so the government would probably settle it in the event of war by passing a general provision, as was done at the time of the Spanish War, to suspend the operation of the tariff law on all materials required by the War Department. There are still only three firms in the country manufacturing the drug—the two already mentioned and the New York Quinine and Chemical Company. Yet the Government might easily elect, if monopoly again threatened to become embarrassing, to establish its own chemical and supply factories—as was done during the Civil War, with a saving to the Government at the Philadelphia laboratory alone of over $766,000 between March, 1863, and September, 1865. As for the supply of the drug to the country—so long as our present coast-line persists a complete blockade seems rather improbable. Yet the quinine problem was a very real one in the struggle between the North and South. If, as Goldwin Smith said in his Manchester speech, the conclusion of the war meant that slavery was dead everywhere and forever this was an achievement worth paying something for. But in estimating the price, do not think only or chiefly of the life lost in the four unfortunate years. Remember as well the disability and debility they left behind them; and in considering the vast financial perplexities which came when reconstruction days began, do not overlook the quinine monopoly which the war had made possible but which a suffering people finally overthrew.

THE IMPORTANCE OF A MICROSCOPICAL EXAMINATION OF ALL GROWTHS REMOVED FROM THE NARES, TOGETHER WITH A REPORT OF EARLY DIAGNOSES OF MALIGNANT GROWTHS.

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The use of the microscope as a means of diagnosis has been much neglected by those especially interested in the diseases of the nose and throat. Jonathan Wright has recently called attention to its value as a routine measure. Beaman Douglas points out that the origin and early symptoms of malignant disease of the nose are wanting and reports a case of primary carcinoma of the inferior turbinated body where the diagnosis would not have been made unless the aid of the microscope had been invoked. Trautmann, in a recent long article on carcinoma of the nose concludes that we must be guided in our treatment by the microscopical diagnosis. According to Pasch the views generally held regarding the infrequency of tuberculosis of the nose will have to be revised. This author has found many cases, which would not have been recognized clinically, as neither the ulcerative nor proliferative forms in which this disease occurs have a characteristic appearance. They are usually of long duration and so are readily mistaken.

However, the lack of an early diagnosis of the true nature of a nasal growth is in no class of cases so serious and sure to lead to evil results, as in the malignant growths. Here the usual distinguishing characteristics are apt to be lacking. When these cases ultimately fall into the hands of the general surgeons with the classical symptoms of growths in this region, such as bulging of the nasal wall and upper jaw, protrusion of the hard and soft palate, exophthalmus, and pressure symptoms, they are either inoperable or do not recover after operation. Bloodgood states that none of these cases have been cured at the Johns Hopkins Hospital and that usually the patients are in a worse state after the operation.

By systematically examining all growths from the nose, these growths will be correctly diagnosed while small and at a time when they can as a rule, be readily extirpated by the nasal route. When this route is not feasible a radical operation can be done, at a time when there is the greatest probability of a cure. Moreover, knowing the nature of the growth removed, we are on the watch for recurrences and are prepared to treat them vigorously.

REPORT OF CASES.

The tissues from the growths described below were fixed in 10 per cent formalin. The sections were stained with hæmatoxylin and eosin.

CASE 1. (History lost.)

Diagnosis.—Mixed cell sarcoma. A small round tumor about the size of a pea, made up of a capsule and the tumor proper. The capsule consists of a loose reticular tissue imbedded in which are numerous polynuclear leucocytes. The tumor proper is composed of round, spindle and irregularly shaped cells. It is rich in blood vessels with walls of a single layer of endothelial cells.

CASE 2. Colored man, age 67 years.

Diagnosis.—Giant cell sarcoma. He complained of nose-bleed and shortness of breath. He had recently been treated in the hospital for mitral insufficiency.

There is no history of cancer in the family. He gives no history of syphilis. Six months ago he began to get short of

breath and four months ago his nose began to bleed, two or three times daily.

On examination of the nose, a tumor mass is seen on the left side blocking up the nares and causing a marked external bulging. From the lower part of the tumor arises a small polypoid mass about the size of a pea. The tumor is of grayish color, firm in consistency, and bleeds profusely on probing. The right nares is atrophic. The post-nasal space is clear. The mucous membrane is pale and atrophic.

Although there was no doubt that here we had to do with a malignant new growth, a small piece was removed for microscopical examination. This patient was seen about six months later and there had been no appreciable increase in the size of the growth.

The tumor is lined by stratified squamous epithelium. Beneath this is a submucosa of connective tissue containing round and spindle shaped cells. The tumor proper has a fibrous capsule which penetrates its substance in places. It consists almost entirely of giant cells each of which contains many nuclei. Between the giant cells are many smaller round cells with small deeply staining nuclei. The tumor is poor in blood vessels which are lined by a single layer of endothelial cells.

Case 3. A. L., female, white, age 29 years.

Diagnosis.—Mixed-celled sarcoma arising from the middle turbinated bone. It might be said here that in view of the history and appearance of this tumor that it was thought to be a polypoid hypertrophy of the middle turbinate, probably of luetic origin.

The patient complained of something in the nose that moved up and down. Her past history revealed that she had had four miscarriages but no other symptoms suggestive of lues. She had noticed something in the right side of her nose for about one week. It obstructed respiration and moved up and down when she blew her nose. She has no pain in the nose nor headache. There is a slight nasal discharge. The nose has bled frequently for the last month and a half.

On examination a pale polypoid growth is seen on the right middle turbinate and a perforation of the septum. Otherwise the examination is negative.

Microscopical Examination.—The tumor is one centimeter long by one-half centimeter broad. It is covered for the most part by stratified columnar epithelium but in one small area there has been a metaplasia to stratified squamous epithelium. The tumor proper is a sarcoma consisting of a mixture of spindle-shaped and round cells, the former predominating. It is very rich in blood vessels, which consist of large spaces with a lining of endothelial cells. Some are empty, some filled with blood corpuscles.

Case 4. H. C., female, colored, age 31.

Diagnosis.—Papilloma on anterior part of septum nasi, showing epithelial ingrowths.

The patient complained of matter falling back into her throat.

No history of any new growth in the family. She has had four miscarriages. Her hair came out in spots last year; no other luetic symptoms.

Her present trouble began about two months ago. The right nostril bleeds when she blows it. When she lies down she has cough and difficulty in breathing.

On examination a papilloma the size of a pea is seen attached by a broad pedicle to the anterior part of the nasal septum of the right side. Removed with the cold snare. The left inferior turbinate is chronically inflamed.

Microscopical Examination.—The tumor is lined by stratified squamous epithelium, cornified in places. It is increased in places to at least a dozen times the normal thickness of mucous membrane in this region. In these areas there are irregular ingrowths into the underlying parts and sections of these ingrowths appear as little epithelial islands. However, the epithelial cells of these ingrowths do not show any irregularities in shape or staining properties. There is no infiltration with young round cells in their neighborhood. The rest of the tumor consists of connective tissue, for the most part rich in cells of an embryonal type closely packed together; in other places these cells are not so closely packed together and here there are many blood spaces.

While one would hesitate to call this tumor malignant, it belongs to a class of cases which should be carefully watched.

The stroma of the tumor is a vascular œdematous connective tissue with few cells and blood vessels.

Case 5.—R. R., male, age 62 years, white.

Diagnosis.—Polypoid tumor in right nares. Microscopical Diagnosis: Nasal polypus of epithelial type with tendency to become malignant.

The patient complained of something growing in his nose.

His family history is negative for any new growth. His past history is unimportant. He has felt the growth in his nose four or five months. It bleeds at times when touched with the finger. For two months the patient has breathed through the mouth at night. He has no pain in the nose or head; has not lost in weight or strength.

On examination a grayish colored firm growth is seen in the right nares, occluding it and apparently coming from the region of the middle turbinate. Otherwise the examination is negative.

After thorough cocainization, preparatory to operation, the growth is seen to come from the bulla ethmoidalis. It was removed in one piece with the cold snare (see photograph). The bulla ethmoidalis was removed with Grunwald's cutting forceps exposing the anterior ethmoidal cells, which appeared normal. The patient was seen a number of times and was finally discharged cured. He was, however, warned of the danger of a recurrence and told to report every few months for examination.

The photograph shows very well the shape of the tumor.

Microscopical Examination. (See photographs.)—The tumor is covered with thick stratified columnar epithelium, the base line of which is thrown into scalloped curves. In places there are downgrowths of epithelium forming alveoli composed of the same type of cells. Some of these alveoli have holes in the centre. The epithelial cells are regular in shape and staining; between the cells are seen many polynuclear cells. There is no infiltration of young round cells about the epithelium.

CASE 6.—A. S., female, white, age 27.

Diagnosis.—Nasal polypi, one of which shows beginning epithelioma. Complained of constant spitting and cough.

Her husband died of consumption 7 years ago. She has been a healthy woman, suffering occasionally from colds and headaches.

Her present trouble began about one year ago. She hawks a great deals and coughs all day long. No pain about the head. Has not lost in weight or strength.

On examination polypi are seen on both sides of the nose in the region of the middle turbinate. The left tonsil contains a small abscess. The larynx is normal. The polypi were removed with the cold snare and one was kept for microscopical study. This is the one showing beginning epithelioma. Seven months later the patient was seen again, when she still complained of hawking and spitting a great deal. On examination of the nares two small polypi were seen, arising from the anterior end of the right middle turbinate. These were removed together with the anterior end of the turbinate with the cold snare, and preserved for examination. A small polypus was also removed from the right nares. These polypi were of a translucent grayish-white color.

Microscopical Examination.—The growth removed at the first operation is of irregular shape, about the size of a large pea. The accompanying photograph gives a very good idea of its structure.

The investing epithelium is of the stratified squamous variety, varying greatly in thickness. As seen in the photograph, it dips deeply into the underlying structure, where it is cut off in places as small epithelial islands. The nuclei of the cells forming these ingrowths vary much in their staining properties, an indication of division. Between the lowermost cells are seen many polynuclear leucocytes.

Just beneath the epithelium is a dense infiltration with small round cells, which is more marked where the ingrowths occur. Deeper down are the acini of numerous mucous glands, imbedded in a fibrous matrix, rich in spindle-shaped cells.

The growth removed at the second operation is about the same size as the first growth. Its epithelial covering varies in variety and thickness. In some places it is of the stratified columnar, in others of the stratified squamous variety. There are no ingrowths of the epithelium but the epithelium shows great variations in thickness, being in places but three layers of cells. In one place where the epithelium is slightly thickened and of the stratified squamous variety there is an infiltration with numerous young round cells.

The tumor proper consists of a loose connective tisue rich in young cells of round and spindle shape. It contains many mucous glands, some of which are dilated (one to a cavity the size of a pin point filled with pink staining material).

In all of the text books on diseases of the nose and throat, the infrequency of malignant growths is noted. Dreyfuss notes 19 cases among 9,554 cases of malignant tumors in various parts of the body. Of these 15 were sarcoma and 4 carcinoma. Among 28,000 patients in Frankel's clinic, Finder found 10 cases of sarcoma and 2 cases of carcinoma of the nose. Darnall mentions having found but 76 cases of carcinoma described in the literature. In an analysis of the literature, Cordes was able to find but eight cases of adeno-carcinoma of the nose. Watson states that there are records of about 200 cases of sarcoma of the nose since the middle of the last century and gives a summary of 150 of these cases.

The form of carcinoma most often found is the squamous-celled variety. Next in frequency are the cylindrical-celled, the medullary form and the adeno-carcinoma. Of the sarcomas, the small-celled, mixed-celled and fibro-sarcoma are most common. According to Watson melano-carcinoma forms 7 per cent of all cases, its occurrence here being next in frequency to melano-carcinoma of the skin and choroid. Moritz Schmidt says, however, that it occurs here very infrequently and that one must not mistake hemorrhages into ordinary sarcoma for it.

The origin of both carcinoma and sarcoma is most frequently on the septum, middle turbinate body and ethmoid bone. Carcinoma originates very frequently in the antrum of Highmore (Bloodgood, Schmidt, Majutin) and gives rise to symptoms of an empyema. Sarcoma rarely arises in the antrum.

Nasal obstruction is the earliest symptom that these growths give rise to. Hemorrhage is often an early symptom, especially in sarcoma. There is usually some nasal discharge. Pain is usually a late symptom and is of a deep boring character. Glandular enlargement and metastases are rarely noted and only when the disease is very far advanced.

In the nose, as elsewhere, sarcoma occurs equally at all ages, whereas carcinoma is usually found after the fourth decade. Sarcoma of the nose pursues a milder course, as a rule, than carcinoma. It is also more amenable to treatment, even when discovered late. Watson reports 39 per cent cured after a radical operation and 54 per cent cured by intranasal treatment. However, it must be noted that in only 28 of the 62 cases reported cured were the histories followed longer than six months. Histories of these cases showed that incomplete operations did not tend to hasten the growth of the tumor (sarcoma) but prolonged life.

Regarding the transformation of benign into malignant growths, Moritz Schmidt is of the opinion that it is possible but that it does not occur frequently. Cobb says that as yet no case has been published that proves this hypothesis.

Sir Felix Semon also holds this view. He has not seen this transformation in over 10,000 cases. Zuckerkandl has not observed this form of degeneration. In his monographs on polypi of the nose, Hopman states that he has observed the combination of polypi and carcinoma but is not prepared to state the relationship. Heymann found that polypi constituted about 10 per cent of all his nasal cases and Zuckerkandl found polypi of the nose in one out of every ten autopsies. Kümmel mentions that as nasal polypi form 2 per cent of all cases of disease of the upper respiratory tract it is not surprising that we frequently find the combination.

However, much is to be said in favor of this hypothesis. In a recent address, von Hansemann states that none of the usually mentioned factors, namely heredity, infection or trauma, can be proved as the cause of cancer. He points out that we must still search for a definite cause. The careful study of this class of cases should aid us in this search. Very few cases, if any, can be adduced that prove this point conclusively. Still there is much evidence to show its probability. As Watson remarks, we know that fibrous and myxomatous tissue become converted into bone, fat and cartilage. Why should they not revert to embryonic connective tissue? In many of the intranasal growths the epithelium is of the squamous-celled variety. This transformation from the cylindrical cell type normally in this region is called epithelial metaplasia and is usually thought due to irritation of the tissue. It is only a step farther for this epithelium to take on malignant tendencies. Heyman regards fibroma, angioma, adenoma, lipoma and epithelioma as modifications of the hyperthrophied nasal mucous membrane.

In Watson's series of 150 cases of sarcoma of the nasal passages, there were 24 cases in which there was a previous history of polypi, that is in 16 per cent. Bloodgood records 18 cases of carcinoma of the antrum, of which five arose in the antrum. Thirteen cases arose from the nasal fossæ, and in 9 of them there was a history of polypi lasting from one to twelve years. Bayer reports a case which strongly supports this form of degeneration. In a man aged 50 years, who had previously been treated for nasal polypi, examination showed a large growth in the upper part of the right nares, the lower part being ulcerated and the upper part having the appearance of an œdematous fibroma. Examination of the excised growth showed the structure of the usual mucous polypus in the upper part, while the lower part was carcinomatous. In Case 6 of our series, it seems most probable that the tumor represents a polypus that has undergone carcinomatous degeneration. No note was made as to which nostril the growth came from. The polypi subsequently removed from this patient were ordinary œdematous fibromata, the epithelium of which, however, had undergone metaplasia and was thickened in places. Heyman described six cases similar to this, which he says might be called benign epitheliomata. He could find no mention of this class of cases in the literature. These growths either arose from the middle turbinated body or in its neighborhood. After removal there was no return in two of these cases after two and three years; one recurred in three years, after which the patient remained well for fourteen years; another case had five recurrences after operation within three years; the fifth also had numerous recurrences during four years, when death intervened from heart failure; the sixth was seen but once. None of these patients had accessory sinus trouble.

In our study of these cases, we must remember that the reverse of this transformation may take place. Hermann reports a case of carcinoma of the antrum, in which a number of typical œdematous fibromata were found in the middle meatus of the nose.

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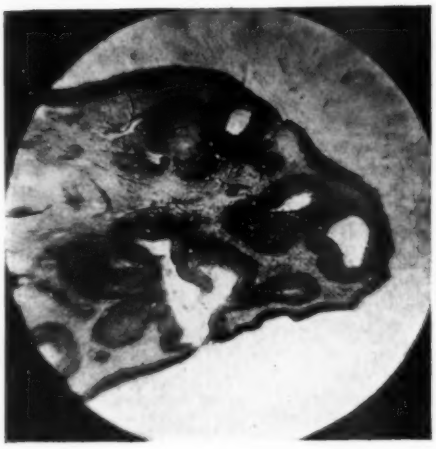

CASE 5.

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CASE 6.

AN EXPERIMENTAL STUDY ON THE RECURRENCE OF LYMPHATIC GLANDS AND THE REGENERATION OF LYMPHATIC VESSELS IN THE DOG.

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The careful anatomical studies (1 and 2) on the axillary lymphatic glands; on the tracheal and bronchial glands (3), and on those adjacent to the common and external and internal iliac arteries (4) show conclusively that we have not the necessary data for a thorough description of the lymphatic glands in man, at the present time. These painstaking studies show that there is a great variation in the size, number and location of the lymphatic glands in a given region, that they are but poorly developed in infancy and tend to disappear with old age. They have also confirmed the belief that the lymphatic glands reach a maximum of development in adult life and that they undergo fatty degeneration and involution at a later age.

Unfortunately, in these studies sufficient account of the modifying influences of disease was not taken. This omission necessarily detracts greatly from their value, for it is manifestly inaccurate to regard as normal what may be abnormal. When we recall how rapidly disease may permanently affect the lymphatic glands it is evident that a statistical study of the size and number of glands is apt to be especially misleading. The influence of either local or general disease makes the whole problem a complicated one. A histological study of every gland seems quite impossible; yet only in this way can we decide to what extent a given gland has in years past been affected by disease. The question as to what is normal is further complicated by the reported fatty involution of glands and by the difficulty of distinguishing between mere accumulations of lymphocytes and true lymphatic glands. In a histological examination of the fat of the axilla of normal individuals Zehnder (2 and 5) found lymph nodules of follicular structure, streaks of lymphadenoid tissue with and without lymph passages, and isolated follicles outside of the true capsule of the gland. Bartel and Stein (6) also speak of lymphadenoid formations in adults, which consist of a collection of lymphocytes with a marginal sinus. These they regard as embryonic stages in which follicles, medullary cords and trabeculæ are not to be found. Glands of microscopical size have also been described in adults by Kling (7). They are found in the walls of the stomach and are known to occur in great numbers in the mesentery.

Aside from microscopical examinations it is not an easy matter to determine what is and what is not a lymphatic gland by ordinary dissecting-room methods. The number of glands found in any region will depend largely upon the acuteness of the observer, the care with which he works, and the age and past history of the subject. In order to locate small glands, special methods of treating the adjacent fat are required. The studies above referred to and some personal observations lead me to believe that in any given region, glands of such varying sizes exist that the smaller ones are recognized only with difficulty by the unaided eye. Only a microscopical examination can reveal the smallest glands and enable us to distinguish between a minute gland which has undergone fatty degeneration and a small fat lobule. That these involuted and small glands and irregular accumulations of lymphocytes have been concerned in the reported recurrence of glands after extirpation and the observed increase in the number of the lymphatic glands in disease, pregnancy and lactation is highly probable.

I. REGENERATION OF LYMPHATIC GLANDS.

A review of the literature on regeneration, recurrence and formation of lymphatic glands in adult life reveals three forms of evidence: clinical, pathological and experimental. In this discussion only the experimental evidence will be considered in detail. The clinically observed recurrence of lymphatic glands after extirpation and their increase in number in such diseases as tuberculosis, malignant tumors, and in such conditions as pregnancy and lactation, naturally led to a series of experiments on animals. These experiments have up to the present, been performed upon dogs and rabbits and consisted in the removal of a part or of the whole of a gland or, *presumably* of all the glands in a given region. Consequently both the question of regeneration and that of the recurrence of glands after resection have been experimentally investigated. The results of these experiments have been very conflicting. To what extent this disagreement is due to the fact that different species of animals of varying ages have been used and that no account was taken of the existence of lymphatic glands of microscopical size, involuted glands and accumulations of lymphocytes it is impossible to say.

Although Bayer (8) published a paper entitled "Ueber Regeneration und Neubildung der Lymphdrüsen" in 1885, the first experiments on regeneration *per se*, were done by Delius (9) in 1888. Delius experimented upon the glandulæ lymphaticæ cervicales superficialis of rabbits. In some cases the glands were perforated by a small knife which was rotated after piercing the gland. In others a wedge-shaped portion of the gland was removed. A piece of catgut was then placed in the defect to mark the seat of the operation. A series of

nine experiments was made, but we are not told how old the animals were, and whether or not account was taken of the catgut, or of hairs from the animals operated on which were accidentally introduced during the operation, and which must have given rise to infection.

From an examination of tissue removed from seven hours to eight days after operation, Delius concluded that regeneration took place by proliferation of elements like those in normal lymphatic glands. Leucocytes appeared in enormous numbers by seven hours, but decreased after the third day. Degeneration of the leucocytes which began by the seventeenth hour reached a maximum by forty-eight hours. After five days leucocytes were found near the catgut only. In every case after seventeen hours mitoses appeared in the fixed tissue elements. Daughter cells of the fixed tissue elements were present by forty-eight hours. These were the only kind of cells which underwent mitoses in the whole process of regeneration. Later the fixed cells of the gland grew into the defect from the periphery, and formed a network which contained mitotic cells and after forty-eight hours, also lymphocytes. Delius conceived the lymphocytes to be pushed forward from the older areas or more probably, to have arisen from the daughter cells of the fixed tissue elements. He reports giant cells near the foreign bodies—hair and catgut.

In 1899 Ribbert (10) repeated these experiments of Delius on rabbits, but chose the submaxillary instead of the superficial cervical lymphatic glands. The operation consisted in the removal of wedge-shaped pieces including one-fifth to one-sixth of the gland. Instead of catgut Ribbert interposed silk thread, pieces of sponge, or pieces of injected lung which had been preserved in alcohol. The age of the animals is again not given, but the histological report is a very complete one. The rabbits were killed from seventy-four hours to five to eight days after operation, when sponge was introduced into the defect; and from twenty-four hours to ten to thirty-six days, when alcoholic specimens of injected lung were so used. The results showed only partial regeneration of the glands with encapsulation of the foreign bodies and the formation of a lymphatic network in small areas of the foreign body. This regeneration Ribbert ascribed to the fixed tissue elements, the endothelium of the lymph-vessels, the fixed cells of the reticulum, to the corresponding cells of the medullary cords and follicles and to the elements of the walls of the vessels. These various elements are said to grow into the foreign body accompanied by blood vessels, where they divide mitotically and form free round cells which transform themselves into lymphocytes. Lymph cells do not take part in the regenerative processes save as some of them may wander in later and help to increase the number of lymph cells found in the newly formed tissue. Ribbert adds that he does not attribute much significance to infiltration by lymphocytes!

The only other experimental study of the question of regeneration is that of Heuter (11). Heuter's experiments were done on the cervical lymphatic glands of dogs with examination of tissues from two to fourteen days after operation. After removal of part of a gland no regeneration, but scar tissue formation was found. Heuter did not interpose a foreign body to mark the defect and for examination used tissue from cases in which healing took place by first intention. He points out that areas of adenoid tissue become isolated by the development of connective tissue into the adenoid tissue surrounding the defect at the expense of the adenoid tissue, in such a manner as to suggest the development of lymphatic tissue. He objects to Ribbert's experiments because a foreign body was introduced, because Ribbert's conception of reticulum was faulty and says that since Ribbert saw the beginning of regenerative changes as early as the fourth day, the picture must have been obscured by the inflammatory reaction following the operation. Heuter also points out that the process of encapsulation of the foreign body, the removal of the pigment from the pieces of injected lung and the presence of giant cells must all have influenced the regenerative processes.

My own observations on the regeneration of lymphatic glands were incidental and quite unimportant; but since they have some bearing upon the question under discussion, I feel justified in reporting them. In my series of experiments on dogs there were two cases of partial excision of a popliteal gland. In these cases from one-half to two-thirds of the gland was removed, in dogs three and four months old respectively. After the skin incision had been made the gland with the fat over it was caused to protrude from the incision by lateral pressure. The incision was then extended to the upper surface of the gland and the latter freed from the surrounding fat by blunt dissection, special care being taken not to injure the afferent and efferent vessels. After from one-half to two-thirds of the gland had been excised what remained was replaced into the wound which was closed by a subcutaneous silver-wire suture. Healing promptly followed and in five days there was little evidence of the operation. By the seventh day in one case and by the tenth day in the other, a deep abscess had begun to form and finally discharged about one centimeter laterally from the line of incision. There was no further trouble and in a few weeks granulation was complete. In the one case in which a histological examination of tissue taken one hundred and sixty-one days after the operation was made, there was no sign of regeneration. Apparently suppuration had destroyed all glandular tissue and healing by granulation may have prevented regeneration from taking place. It is evident that in both of these cases the infection must have been secondary. It seems probable to me that this arose through infection of the lymph which had exuded from the cut surface of the gland for no such result as this followed any of the other operations. When infection occurred in these it was always in the skin incision itself, never in the depth of the wound, and followed promptly after operation.

So far as regeneration in the cervical and submaxillary lymphatic glands of *rabbits* is concerned we must conclude from these experiments of Delius and Ribbert that the question is still an open one. Delius and Ribbert observed regenerative processes as early as the fourth day after operation,

without taking any account of the inflammatory reaction following an operation which included the introduction of catgut, and hairs from the animals operated on in Delius's cases. Besides, the histological report is not convincing and does not agree at all with that of Heuter. Ribbert, who reported only partial regeneration by thirty-six days, also failed to lay sufficient stress on infiltration and the presence of a foreign body. Besides, as Heuter has pointed out his conception of reticulum was faulty and we may add that his opinion as to the origin of lymphocytes has not been confirmed.

In dogs we can, I think, accept Heuter's experiments as conclusive for the dogs operated on. No foreign body was introduced and the histological report is very satisfactory. It must be remembered that regenerative activities might be present in young dogs but absent in older ones and even if regeneration does not occur in the dog it may do so in the rabbit. In any study on regeneration it is of great importance to consider the age of the animal operated on and its place in the animal kingdom. Studies in regeneration although conflicting, have shown quite clearly that these powers are more active in the lower orders and the earlier in embryonic or post-embryonic life that the experiment is performed. They may indeed be present in early life and absent later, and that regeneration may be present in principle even when its capabilities are insignificant, seems to be indicated by the studies on regeneration of the epithelia of the larger gall ducts and by the regenerative activity observed in ruptured human livers by Orth and Heile.

II. Recurrence of Lymphatic Glands.

Bayer (8) (in 1885), undertook the first experiments on the recurrence of extirpated lymphatic glands in the axilla of the dog. The age of the dogs varied from two weeks to several years and the interval between operation and death from several weeks to four months. Bayer removed all the axillary lymphatic glands after the injection of India ink. Before killing the animals cinnabar was injected in order to distinguish the newly formed glands from those left after operation. In the first dog which was one and a half years old, changes in the fat were noticed six weeks after operation around the places stained by India ink, at the seat of operation. From these changes Bayer says we must assume a change from fat to connective tissue cells and further asserts that the sheaths of the vessels give off the material for the formation of new lobules of fatty tissue. The fact that more cinnabar than India ink is found in the glands is taken as an evidence of the young stage of the glands.

In the second dog the result was a negative one. This Bayer attributes to healing *per secundam* and to the enlargement of the collateral lymphatics by which means stasis, the main impulse to regeneration was prevented. From these two contradictory experiments the following conclusion is reached. After removal of lymphatic glands recurrence takes place in a comparatively short time from the surrounding fat unless a collateral lymphatic circulation develops or healing takes place by granulation.

In 1886 Bayer (12) elaborated his views from a study of diseased glands which he conceives to impede the flow of lymph, cause dilatation of lymphatic vessels, saturation of the surrounding tissues, secondary emigration of lymph cells and proliferation of cells in circumscribed areas near blood and lymph vessels. These latter areas are later transformed into follicular structures through cell activity.

In 1891, Bayer (13) developed his theory of the formation of lymphatic glands from fat still further from a study of the phenomena observed in adjacent fat after extirpation of tumors. At the outset of the paper the author states that the opinion of Klein (15) that adipose tissue really belongs to the lymphatic system and is to be considered as changed lymphatic tissue, won more and more truth with him. From the examination of an extensive cavernous lymphangioma Bayer says he is able to confirm and to extend his former observations. He traces transitions from fat to endothelium of lymph spaces and says that the capillaries are in some places surrounded by accumulations of cells which are formed not only by proliferation of cells of the adventitia but by proliferation of fat cells as well. These accumulations he further considers as having a possible origin in the cells of the sarcolemma and he regards it a proven fact that adventitia cells can give rise to fat cells at one time and furnish material for new blood vessels at another time.

In 1895 (14) Bayer says that since *experimentation introduces unavoidable obstacles to a good observation of the facts*, he has confined himself to the examination of glandular tumors such as lymph-angiomata and angiose-lymphomata. The following reasons are given for the recurrence of lymphatic glands: (1) lymphatic glands lie in fat; (2) glands and fat lie as a separate whole; (3) disease of the glands is accompanied by striking macroscopical and microscopical changes in the surrounding fat; (4) total destruction of lymphatic glands by disease leads to a decrease of fat; (5) the number of glands increases *pari passu* with the decrease of fat; (6) unmistakable pictures of newly formed glands in all stages of development can be found; (7) the surrounding fat contains separate lymph channels which are in communication with those formed pathologically and with the lymph channels of glands; (8) changes occur in the fat surrounding lymphatic glands, which must be considered regenerative. Bayer also reports a direct communication between lymph clefts lined only by fat cells and the lymph channels and says he has traced the transition from fat cells bounding these clefts to perfect lymphatic glands. He adds, however, that the complete process only occurs under propitious circumstances.

I have reported Bayer's work at some length in order to show that his main evidence is not experimental but pathological. While fully aware that pathological and physiological regeneration have been shown to be practically identical and that pathological regeneration is thought to be only an enhanced and modified physiological regeneration following

either mechanical injury or disease, yet, it seems to me, granting that Bayer's observations are correct, his error lies in the assumption that regenerative processes which may be present in pathological states, are also present normally. That this is not the case Bizzozero (16) has well expressed in the following words: "Wenn sich die Verhältnisse ändern und gewisse pathologische Zustände eintreten ändert sich auch die Regenerationsthätigkeit und kann auch an solchen Orten sehr lebhaft werden wo sie normal nicht zu finden ist."

Number of the dog	Age	Interval in days	Nature of the healing	Region operated upon	Side operated upon	Nature of operation
I.	2-3 yr.	7	Per primam	Mesent	Both	One gland 35x6x5 mm removed.
II.	3-4 yr.	91	Per primam	Mesentery	Both	Two glands removed on each side. R. S.—48x12x8 and 6x8x5 mm. L. S.—40x8x8 and 32x10x8 mm.
IV.	6 mo.	25	Per secundam	Popliteal	Right	One gland and one third of surrounding fat removed.
			Per primam	Popliteal	Left	Two glands and no fat were excised.
V.	3 mo.	161	Per primam	Popliteal	Right	One gland and most of the fat was removed.
			Per primam	Popliteal	Left	Two-thirds of the gland only was removed—abscess after seven days.
VI.	2-½ mo.	89	Per secundam	Popliteal	Right	All (?) the fat and glands were removed.
			Per primam	Popliteal	Left	Gland only was removed. A piece of the capsule remained.
VII.	4 mo.	53	Per primam	Popliteal	Right	Gland only was removed. Animal lost.
			Per primam	Popliteal	Left	One-half of gland removed—abscess after ten days.
VIII.	3-½ mo.	85	Per primam	Popliteal	Right	Gland and fat removed.
			Per primam	Popliteal	Left	Gland only removed.

The table above gives a summary of the experiments on the popliteal and mesenteric glands.

Through the suggestion of Prof. Sabin, a number of experiments on the lymphatics were undertaken in order to obtain, if possible, additional evidence on these questions. These experiments included the extirpation of lymphatic glands and the resection of lymphatic trunks in dogs from two months to several years old. In two cases the large glands lying at the root of the mesentery near the spinal column were removed and in seven instances the popliteal glands were extirpated. Although the lymphatic system of the dog (17) is not highly developed, one and occasionally two, palpable glands are found in the popliteal region.

The difficulties necessarily associated with abdominal operations caused me to choose the popliteal region as especially adapted to my purpose. The operation here was less severe, the seat of operation was not hidden from view by adhesions between coils of intestine after operation, a more complete extirpation was possible, the area drained by the removed glands could easily be ascertained, the progress of healing could be better observed and the nutrition of the animal was not disturbed. In these operations the ordinary surgical technique was adopted and every care was exercised to prevent infection. Where infection did occur a special note was made and account was taken of this fact in the histological examination of the tissue. Daily notes were made on the condition of the wounds and the state of health of the animals.

In four cases the popliteal glands and all the fat in the popliteal region were removed as thoroughly as possible. This could easily be done as deep down as the popliteal vessels. In three cases the gland with the overlying fat was caused to protrude by pressure from the skin incision and the gland freed by blunt dissection from the surrounding fat after the necessary superficial incision into the overlying fat. In these operations especial care was exercised not to disturb the adjacent fat because Bayer laid considerable stress upon this fact. The skin incision was closed by a subcutaneous catgut, silk or silver suture and a sterile dressing was applied. The afferent and efferent lymphatic vessels were not ligated.

From the table opposite it will be seen that the intervals varied from seven to ninety-one days in the two abdominal operations, and from twenty-five to one hundred and sixty-one days in those on the popliteal glands. So that for all practical purposes we have an interval of experimentation varying from twenty-five to one hundred and sixty-one days. An earlier examination of tissue than twenty-five days seemed unnecessary to me since it hardly seems possible that the evidences of attempted regeneration would not be visible after three and a half weeks if present at an earlier day. If regeneration had occurred a later examination would have revealed this as well as an earlier one, while it would not have had to reckon with the inflammatory reaction following injury. The nature of the operations varied from partial excision of fat and glands to as complete an excision as possible. If we exclude those cases in which healing took place by granulation and the two instances in which a part of the gland was left *in situ*, there remain five operations on the popliteal glands and two on the mesenteric glands against which no objection can be urged. In three out of five operations on the popliteal glands the gland or glands and no fat were removed. In two cases the gland or glands and all the fat possible, were removed. In the abdominal operations the glands only were removed by blunt dissection.

Before killing the animals they were etherized and the lymphatics of the extremity injected from the pad of the foot with India ink, as far as the inguinal and lumbar glands. In several cases the animals were bled to death after injection of the lymphatics and half a litre of one per cent formaline

injected into the aorta. These animals were then skinned and the bodies placed in five per cent formaline for two days, after which they were transferred to alcohol. In other cases the fat with the contained lymphatics was removed *en masse* from the popliteal region, spread on wax and fixed in formaline. In every case the fresh tissue was carefully examined macroscopically as to the condition of the injected lymphatic trunks and the presence of small glands. After fixing and hardening, the tissue was cut into blocks of convenient size, imbedded in celloidin and cut 10-30 microns thick, each tenth section being stained and mounted. All sections were preserved, however, and more were stained as required. In some cases every fifth section was examined.

Such an examination of the tissue in three out of the five experiments on the popliteal glands showed no evidences whatever of the presence of lymphatic glands or of lymphatic nodules. In those cases in which total excision of the fat had been done the amount of fat found post mortem was much smaller but the histological picture was exactly the same as in those in which only part or none of it had been removed. In two of the five cases of extirpation a small gland was found. In one of these operations the gland only, while in the other case, both gland and fat had been removed. One of these specimens was from a dog two and a half months old at the time of operation. Healing was by first intention, the interval was eighty-nine days, and a piece of the capsule of the gland was left *in situ*. This remnant was plainly visible in the sections, but there was no lymphatic tissue in the neighborhood of it. The gland which was found, lay in a distant part of the section; it had the appearance of a mature gland and was surrounded by a definite capsule of connective tissue. This gland was about 3x2½ mm. in size, and the fat around it showed no infiltration or other changes indicative of active regenerative processes of any kind.

The small gland found in the other case looked also like an adult gland, or rather follicle. There were evidences of degeneration in the center and the gland lay in a mass of connective tissue which showed no signs of cellular proliferation. This gland which was only one millimeter in size also lay distant from the seat of operation. On referring back to my memoranda I found the following note made on the fifth day after operation: "On the left hind leg a nodule about seven millimeters in size is felt in the depth of the popliteal region. It is hard and shot-like and suggests an enlarged, unremoved gland." Aside from the value of this note the fact that no regenerative changes were found in the regions from which the glands had been removed seems to indicate that we have to deal with unremoved glands. The existence of glands of microscopical size and of irregular masses of lymphatic tissue in man has already been referred to. There seems to be no good reason why these may not exist in the case of dogs, and especially in young dogs. In order to determine whether or not small glands are commonly present in the popliteal region of dogs, the popliteal fat was removed in eight dogs, from two to four years of age. This fat was pinned on wax, all blood was removed by washing, and fixed in formaline. After hardening in alcohol the specimens were cleared in creosote and xylol and some in oil of bergamot. An examination by means of the dissecting microscope revealed five small lymphatic glands from 3-6 mm. in size, in these sixteen specimens. From these facts it cannot be doubted that still smaller glands are equally common. It may be recalled that Arnold (18) has shown that accumulations of round cells which look like small follicles, are found normally in rabbits and dogs in the interacinous bands of connective tissue about the gall ducts. If such be the case it is evident that complete extirpation of the lymphatic glands of any region is quite impossible and that the small glands found in the above cases were most likely unremoved mature glands and not newly formed ones. Since also none of the specimens in which healing took place by granulation showed any signs of regeneration or recurrence, I feel justified in concluding from this and from the above facts that in these seven instances of extirpation of the popliteal glands there was no recurrence.

In the two cases of abdominal operation in which the large lymphatic glands lying in the root of the mesentery of the small intestine were removed by blunt dissection, the condition of the intestine was a very interesting one. The glands removed were approximately 3x1x1.5 cms. and drained all of the small intestine save the duodenum and all of the large intestine save the rectum. In neither of these cases was there any ascites or sufficient disturbance of nutrition to cause an unusual loss of weight in the animals. Indeed, in one of the dogs there was a steady weekly gain in weight of one-half to two pounds after the first week.

Upon opening the abdomen of the first dog seven days after operation, the folds of the mesentery of the small intestine were matted together and the omentum was adherent to the small intestine and mesentery. On gently breaking the adhesions little pockets of chyle were found. The omental adhesions had sealed off the cut ends of the peripheral lymphatic ducts and evidently prevented the escape of chyle into the peritoneal cavity. The wall of the intestine was œdematous along the mesenteric border. Injections of Prussian blue into the walls of the small intestine could be followed to the seat of operation but never went into the receptaculum. The latter could be injected from the duodenum, however. The thoracic duct was distended with lymph and not with chyle. These injections seem to show that the central ends of the lymphatic ducts had not been regenerated. Tissue taken from the seat of operation showed a typical picture of a granulating wound. There were no evidences of regeneration of the removed lymphatic glands but there was an intense infiltration.

The other dog on which a similar operation was made was killed eighty-four days after operation. In this case, too, there was no ascites and no loss of weight beyond that following any abdominal operation. The omentum was found adherent to the parietal peritoneum along the linea alba and the adjacent coils of small intestine were firmly adherent to each other in numerous places near the seat of operation.

No pockets of chyle were found though the dog had been fed milk before the killing, as a result of which the intestinal lymphatics and the receptaculum were well filled with chyle. Owing to the manipulations made necessary by the adhesions these naturally injected lymphatics could not be traced to the seat of operation. However, injections of Prussian blue made from various parts of the small intestine under ether, seemed to show a direct connection with the receptaculum. In some cases the injection seemed to run across the seat of operation and in one case an injected duct was traced from the ileum to the duodenum. After all the injections had been made the viscera were fixed *in situ* by the intra-arterial injection of a one per cent solution of formaline.

The histological examination of the tissue from the seat of operation showed small lymphatic glands present in some of the sections. These glands were always enclosed in a definite capsule which was sharply delimited from the surrounding fat. They did not lie at the places where the granulation tissue was found and had all the appearances of mature glands. There were no signs of cellular proliferation. Consequently it seems probable that these are also small glands which existed previously to operation and which are so numerous in the mesentery; or small lymphatic nodules which lay outside of the capsules of the removed glands. Although, in my opinion, all these experiments on dogs were negative so far as recurrence of lymphatic glands is concerned, such recurrence may take place in younger dogs or in case of disease. As pointed out above, the only *experimental* evidence of such recurrence is the one case in a dog one and a half years old, reported by Bayer. Bayer's second case was negative and against his first case serious objections can be urged. Besides, although Bayer reports having operated on a series of dogs whose ages varied from two weeks to several years, the rest of the series are not reported.

It does not seem probable to me that recurrence is likely to occur after years, unless in disease, if there be no signs of recurrence in five or six months. Regenerative processes, when they do occur, have been shown to take place *pari passu* with the repair of the injury. Both the blood supply and cellular activity are greatest at this time, obstacles to growth are absent, a collateral circulation has not developed, and other organs have not assumed a vicarious activity. When granulation is complete the granulation tissue would seem to interpose an obstacle to regenerative processes and in the case under consideration both injury and stasis are absent as stimuli.

III. Regeneration of Lymphatic Vessels.

The injections of Prussian blue into the intestine in one case of resection of the mesenteric glands already referred to, seemed to indicate that the severed lymphatic trunks had after eighty-four days or previously, re-established central connections with the receptaculum. I say seemed to indicate, because it is impossible to say whether or not some lymphatic vessels remained uninjured on the outside of the gland when the latter was removed by blunt dissection. It is also probable that small blood vessels were injected, for the study of the sections from the seat of operation show many blood vessels containing injection material.

In order to test the question of regeneration of the larger lymphatic vessels by actual experiment a series of sections and resections were done on the large lymphatic trunks lying on either side of the saphenous vein, near the knee of the hind leg of the dog. Preparatory to operation the lymphatics of the hind leg of the dog were studied by means of injections of Prussian blue, methylene blue and India ink. By these methods it was found that twenty-five minims of a one per cent solution of methylene blue when injected into the pad would make the main lymphatic trunks plainly visible.

Before making the skin incision at the time of operation, a sterile normal salt solution containing one per cent methylene blue was injected into the pad of the foot. One and sometimes two, of the largest lymphatic trunks lying just anterior to the saphenous vein in the region of the knee were then ligated with black silk thread and cut between ligatures, in four cases. In four other cases from 3-5 mm. of the trunk was resected between the seat of the ligatures. The skin incision was closed by a subcutaneous catgut or silk suture and a sterile dressing applied. There was never any œdema of the leg below the seat of operation save when the dressings had been applied too snugly. The following table summarizes the operations with results, as found by injections after killing the animals and by microscopical examination of the tissue.

Dog	Age	Interval in days	Healing	Region	Operation	Result
III.	4 yr.	91	Per primam	Left hind leg	Resection of largest trunk	No regeneration
....	....	91	Per secundam	Right hind leg	Section of largest trunk	No regeneration
....	....	14	Per primam	Left front leg	Resection of largest trunk	No regeneration
....	....	14	Per primam	Right front leg	Section of largest trunk	No regeneration
VI.	2-1½ mo.	84	Per secundam	Left hind leg	Resection of two trunks	No regeneration
....	....	..	Per primam	Right hind leg	Section of two trunks	No regeneration
VII.	3-1½ mo.	27	Per primam	Left hind leg	Resection of largest trunk	No regeneration
....	....	27	Per primam	Right hind leg	Section of largest trunk	No regeneration

In these experiments the intervals between the time of operation and the death of the animals varied from fourteen to ninety-one days, and the age of the animals from two and a half months to four years. In two out of the eight cases healing was by granulation, in six by first intention. After etherizing the animals preparatory to killing, 10-20 cc. of Prussian blue or India ink were injected into the pad and the

leg alternately flexed and extended while the pad of the foot was massaged, in order to assure a thorough injection. In some cases the dog was then bled and a solution of formaline injected intravascularly. After fixation the skin of the leg was removed and the condition of the lymphatic trunks especially noted. In all cases the ligated and resected lymphatic trunks were distended with the injection fluid up to the seat of operation, but never across the same. The injection of the resected trunks above the seat of operation was always accomplished through the collateral subcutaneous and anastomosing vessels. The accompanying lymphatic trunks were usually found considerably larger near the seat of resection than at the time of operation even when only the same amount of injection fluid was used as at the time of operation.

The tissue including the saphenous vein and the three large accompanying lymphatic trunks, at the seat of operation, was excised and after the usual procedures cut 10-30 microns thick, in celloidin. Four specimens were examined in series and four by staining every fifth or tenth section. All unstained sections were preserved, however. The presence of the black silk ligature made it easy to recognize the exact seat of the operation in the sections. The resected or sected lymphatic trunks could never be traced across these regions and were often found with thickened walls in an obliterative condition. The results of the histological examination agreed entirely with those of injection and were exactly the same whether section or resection had been done. Around the ligatures there was an intense accumulation of lymphocytes and leucocytes such as is characteristic about encapsulation of a foreign body in granulation tissue. Regeneration of lymphatic trunks was found in no instance. It may be urged that the silk ligature being a foreign body may have interfered with the process of regeneration. This may be so; yet in all the operations on the popliteal glands the afferent and efferent trunks which were always cut close to the hilum of the gland were never ligated and still it was never possible to inject these large trunks across the seat of operation. The large afferent lymphatic trunk could always be traced into the fat in the popliteal region, but the injection never extended across the gap left by the removal of the glands, to the efferent part of the same trunk. Since there were eleven such operations it seems quite probable that if the silk ligature had been the only obstacle to regeneration, connection between the cut ends of the lymphatic trunk in the popliteal region would have been re-established in some cases at least.

If stasis be the main stimulus to regeneration it is quite probable that resection and ligation of one or two principal trunks in the region of the knee and elbow did not interpose sufficient obstruction to the flow of lymph. This can hardly have been the case in the operations on the popliteal glands, however, for here all the large trunks of the hind leg converge to form a single trunk. Consequently, all the superficial lymph from the lower extremity must have been carried past this point of obstruction by the numerous small lymphatics of the skin. Further experiments in which all the superficial lymphatics of an extremity are divided have been undertaken, and it is hoped that some evidence bearing on the question of regeneration of the larger lymphatic trunks and of the formation of lymphatic channels in granulation tissue may be obtained.

The fact that in these experiments the large lymphatic trunks have, in all respects, acted like blood vessels under similar conditions makes it probable that the capillary lymphatics act similarly also in the case of a granulating wound. Talke (19) found epithelial tubes which he recognized as lymphatic vessels, in the adhesions about the ascending colon in a case of perityphlitis and in a case of thickened pleura. In the latter Talke could trace branches from the visceral subpleural lymphatics into the pleural thickening. These newly-formed lymphatic capillaries joined the old lymphatic vessels and extended in the general direction of the blood vessels. They were composed of epithelial tubes from 6-10 microns in diameter, which in some cases contained lymph, coal dust and pigmented leucocytes. Although Talke was not able to see the mode of formation of these lymphatic sprouts because of the absence of sufficient granulation tissue in his specimens, he thinks that the new formation of lymphatics proceeds as in case of the blood vessels, from the pre-existing lymphatic vessels. Further evidence of a similar nature is offered by Behre (20) in a case of tuberculosis in which coal pigment *seems* to have been carried across a much thickened and densely adherent pleura. However, these pathological evidences, though valuable and suggestive need verification, before we can accept the formation of lymphatic vessels in granulation tissue as a fact. As far as I am able to learn, such experiments have not yet been done nor can I find any reference in the literature to experiments on the question of regeneration of lymphatic trunks such as reported here.

It is a pleasant duty to acknowledge my indebtedness to Prof. Mall for his interest and many suggestions.

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NOTES ON NEW BOOKS.

Distribution of the Cells in the Intermedio-lateral Tract of the Spinal Cord. By ALEXANDER BRUCE, M. D. XLV, 105-131, 1 pl. (*Reprinted from the Transactions of the Royal Society of Edinburgh, 1906.*)

Professor Bruce has increased the debt of neurologists to him by adding to his well-known atlases of the medulla and spinal cord the present study, which deals with the exact distribution of the cells in the intermedio-lateral tract of the spinal cord. This intermedio-lateral tract, first so designated by Lockhart Clarke, and the adjacent cell-groups have long interested investigators of neural anatomy. The studies of Waldeyer and of Argutinsky will be especially recalled. No one had, however, worked out carefully, by modern methods, the exact distribution of the cells in the tract.

Bruce has examined serial sections from the upper part of the cervical enlargement to the lower extremity of the spinal cord, studying in all some 7000 sections, of which more than 5000 contained cells of the intermedio-lateral tract. These cells, as found on both sides of the cord, were carefully counted independently by four different observers. The study illustrates the topography in the various segments. It proves that the intermedio-lateral tract is present in the upper cervical region, in the lower cervical, thoracic and upper lumbar regions and in the lower sacral region, though it is absent in the cervical enlargement from C.5 to C.7 and in the lumbo-sacral region from L.3 to the upper part of S.3 inclusive. It is interesting that the middle cells described by Waldeyer do not form any part of the intermedio-lateral tract. Bruce's counts show some 89,000 cells in the tract on each side. The cells do not form a continuous column, but occur in groups or clusters. The distribution on the two sides may be asymmetrical. There appears to be a remarkable increase in the number of cells of the tract in the third thoracic segment. The vascular supply to the tract is said to be largely independent of that of the motor cells of the anterior horn.

Though Bruce's study is anatomical, he comments upon the physiological function of the cells, and points out that where there is the greatest outflow of sympathetic fibres from the cord, there the number of cells in the intermedio-lateral tract is greatest. He mentions the suggestions of Anderson and Herring and of Onuf and Collins that the intermedio-lateral tract is the source of the sympathetic fibers, but he feels that further researches are necessary before anything definite can be said on the subject.

There is as yet scarcely any pathology of the intermedio-lateral tract. It escapes entirely in cases of chronic degeneration of the anterior horns, such as occurs in progressive muscular atrophy and in amyotrophic lateral sclerosis. In one case it has been found to be degenerated in connection with erythromelalgia. Bruce expresses the hope that future research will succeed in explaining symptoms of visceral and vascular diseases hitherto imperfectly understood. L. F. B.

Lectures on Auto-intoxication in Disease, or Self-Poisoning of the Individual. By CH. BOUCHARD, Professor of Pathology and Therapeutics, with a preface and new chapters added. Translated by THOMAS OLIVER, M. A., M. D., F. R. C. P. Second Revised Edition. (*Philadelphia: F. A. Davis Company, Publishers, 1906.*)

The publication of a second, revised translation of Professor Bouchard's book shows that there has been a demand for it, which may be regarded as a testimonial of its value. The reviewer does not feel, however, that this demand is justified by the character of the book. Its success simply proves that the medical profession has not completely outgrown a love for the metaphysical and theoretical. It is because it is so much easier to think than to try, and so much more simple to accept elaborate reasons ready made than to scrutinize proofs carefully that this book appeals to so many. The terms uric acid diathesis and auto-intoxication have furnished so many with material to glibly cover what they don't know that it may seem cruel to try to deprive still others of this comfort. So much semi-scientific work of this sort has come from American sources and this has been so often held up against us that it is a true pleasure to know that this book has been written by a professor in the University of Paris and that he has permitted its republication after ten years.

The main experimental work from which the broad and far-reaching conclusions are drawn is the writer's well-known work on the toxicity of the urine as tested by injection into animals. It is to the credit of the translator that he has introduced some of the criticisms which have been uttered against Bouchard's work. Interesting and valuable as it has been because stimulating to further and more accurate work, it by no means possesses the importance or justifies the conclusions given to it by Bouchard.

A great many allusions are made to the scientific work of others, but as no accurate references are given, the book has no value as a reference book on abnormalities of metabolism. It would be useless to quote many of the absurd theories which the book contains, such as the series of ills which are believed to follow in the train of dilatation of the stomach. "Chlorosis in young girls and pulmonary phthisis are often induced by dilatation of the stomach." There is even thought to be a close relationship between "nodosites on the second articulations, dilatation of the stomach and typhoid fever."

"The healthy man is both a receptacle and a laboratory of poisons. In fact, he receives them in his food, he creates them by dissimilation, and he forms them in his secretions."

Truly, one may say with Sir Thomas Browne, that "men . . . quarrel with their constitutions for being sick; but I . . . do wonder that we are not always so."

No one can deny the grains of truth upon which this book is built, and we recognize the important rôle which organic poisons play in disease, but this book does not approach these problems in any scientific or national spirit.

It will only aid in keeping alive and spreading the *theory* of auto-intoxication, about which we have already heard too much in internal medicine.

Christianity and Sex Problems. By HUGH NORTHCOTE, M. A. *(Philadelphia: F. A. Davis Company, 1914-16 Cherry Street, Publishers, 1906.)*

The author deserves much credit for approaching a difficult subject with delicacy and dignity. His aim throughout is to benefit the young and his standpoint is of the highest, in refreshing contrast to much of the pornographic literature of the past two decades. It is to be feared, however, that he underestimates the degree to which the comparatively young become informed upon these forbidden topics through the traditions of schoolmates and servants. If the book is designed for the young it should be simpler in style and less ambitious in treatment. When persons have reached an age to appreciate and profit by a semi-religious and philosophical treatise upon sex relations their habits and views are generally well-fixed. The book, however, will be useful to teachers and helpful to those who have the responsibility of the moral training of aggregations of young people. It contains many valuable chapters.

The National Standard Dispensatory. Containing the natural history, chemistry, pharmacy, pharmacopœias of the United States, Great Britain and Germany, with numerous references to other foreign pharmacopœias. In accordance with the United States Pharmacopœia, 8th decennial revision of 1905 by authorization of the Convention. By HOBART AMORY HARE, Jefferson Medical College; CHARLES CASPARI, JR., Maryland College of Pharmacy; and HENRY H. RUSBY, College of Pharmacy of the City of New York. Imperial octavo. *(Philadelphia: Lea Brothers & Co., 1905.)*

This ponderous volume of 1860 pages arrayed in magnificent calf, high tribute to the bookbinders' art and a distinct credit to its publishers in paper, type and editing, supersedes the "National Dispensatory" of Stillé & Maisch, which for a quarter of a century held sway as a standard work on the botany, chemistry and therapeutics of drugs and medicines. None of the original editors are now alive, and while in its previous edition Professor Charles Caspari, of Baltimore, was associated with Messrs. Stillé & Maisch, the present work is the product of the efforts of Professors H. A. Hare of Philadelphia, who edits the therapeutical portion, Charles Caspari, Jr., of Baltimore, who edits the pharmaceutical and chemical portions, and H. H. Rusby, of New York, who edits the botanical portion. These are assisted by Messrs. Edward Kremers, of the University of Wisconsin, Daniel Base, of the University of Maryland, and Joseph Geisler, of the New York State Department of Agriculture.

As the U. S. Pharmacopœia, 1900, is a decided improvement upon and change in its predecessor, the Pharmacopœia of 1890, so this Dispensatory, based as it is upon the new Pharmacopœia, is a distinct advance and improvement upon its predecessor, the National Dispensatory. The most marked feature of difference is practically the entire elimination of the old part of the former edition. It had been the custom of former editions to let the old views it contained remain and merely add modern views, so that the book throughout was a symposium of views upon the chemistry, therapeutics, etc., of drugs from time immemorial almost down to the present day. As the present views of scientists of half a century ago upon therapeutics in the past interest us little except in an historical way, it seems wise of the present editors to eliminate the antique from their work. The prime purpose of a Dispensatory is to serve as a commentary upon the Pharmacopœia, inasmuch as the latter gives no why's and wherefore's, and the raison d'être of many of its statements and methods and conclusions is not clear to the average practitioner of medicine and pharmacy. Our first Pharmacopœias were hence not used to any great extent and it was not until the Dispensatory was born that the Pharmacopœia became as it should be a vademecum to doctor and druggist.

The Dispensatory contains all that the Pharmacopœia contains, but explains each step of the latter in a readily intelligible form, and besides volunteers information upon all kindred subjects not contained in the Pharmacopœia. While for instance the Pharmacopœia contains only a small portion of all the plants, animal products and chemicals that are used in medicine, the Dispensatory attempts to, and in the main succeeds in bringing to our attention all drugs that are used anywhere in the civilized world, certainly all that are used in this country. As old drugs are continually becoming new and popular in use while new ones are dropping by the wayside, it is apparent how important it is to have at hand a work which will supply us with desired information upon any drug we may be looking for or intending to use. The general arrangement of the book is alphabetical and a perfect index makes finding the subject sought a very easy task. The Latin title prevails in all cases as the heading, followed by the English title and then the French and German title. Then follows a description or formula of the article, and thereafter its preparations, then its properties, then tests for its purity or assay methods for determining its strength and finally its therapeutical action and uses and its dose. Under any given drug all of the preparations which contain it are also given. Besides this substitutes and adulterants are also treated of in each case as a warning to the uninitiated in the all-too-much practiced arts to-day of the "just as good" and of the sophisticator.

While all the assay processes for the standardized drugs of the Pharmacopœia are given in full it would have been desirable to add in some instances explanatory remarks as to the reasons for certain steps and processes, which to the unskilled practitioner must be more or less mysterious. The idea of arranging various members of one plant family under the head of that family is an acceptable innovation and will meet with deserved approbation no doubt. The illustrations throughout the work appear to be new and specially drawn and are very creditable. The microscopical drawings of cross sections of leading drugs also add to the value of the book as a means of determining the genuine from possible adulterations or spurious drugs. The chemical and pharmacognostical part of the book is well written and thoroughly up-to-date, while the botanical part reflects a close study on the part of the editor of the most modern research on botany. A special chapter is devoted to physiological testing as an innovation in this book, and while it cannot be claimed that standards of drugs can be definitely established by animal experiments, still in cases of those drugs whose chemistry is insufficiently developed to warrant a chemical standard of strength, such as ergot and cannabis, it may be said that such a physiological test standard is better than none at all. The appendix like that of the Pharmacopœia is very extensive and follows the latter pretty closely, embracing reagents, test solutions, volumetric solutions of all kinds, and how to use them, saturation and solubility tables, molecular weights, equivalents of weights and measures in the avoirdupois, apothecaries and metric systems, alcohol and specific gravity tables, weight and volume relations and thermometric equivalents. In fine, the National Standard Dispensatory unquestionably presents the best work of its kind that has yet been published, combining fully the accuracy and thoroughness of the best German works with American completeness.

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